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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,905	11/02/2001	Susan Schwendner	018781-007210US	9747

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EXAMINER	
KRASS, FREDERICK F	
ART UNIT	**PAPER NUMBER**
1614	7

DATE MAILED: 09/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/052,905	SCHWENDNER ET AL.	
	Examiner	Art Unit	
	Frederick Krass	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Election of Species Requirement

Upon reconsideration, the election of species requirement is withdrawn.

Written Description Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant specification fails to provide an adequate written description of "proliferative disorders" generally. The specification describes only a limited genus of proliferative disorders, i.e. cancer and psoriasis (see page 2, lines 15-19 of the instant specification). No other particular "proliferative disorders" are disclosed. Under these circumstances, Applicant's claiming "proliferative disorders" broadly, with no specific pathologies being specified, is merely "a mere wish or plan" for treating such diseases in the future, not an adequate written description of treatment, which would require

specifying diseases and detailing specific treatment regimes. See generally, Univ. of Rochester v. G.D. Searle & Co., 249 F. Supp.2d 216, 225 (W.D.N.Y. 2003).

Scope of Enablement Rejection

Claims 11-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treament of mammary cancer with a combination of a pentafluorobenzenesulfonamide and gemcitibine/paclitaxel, does not reasonably provide enablement for the treatment of "proliferative disorders" generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled

artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth hereinbelow.

1. The nature of the invention, state of the prior art, relative skill of those in the art, and the predictability of the art

The claimed invention relates to chemotherapy, and the relative skill of those in the art is high, generally that of a PHD or MD. This unpredictability has a number of facets, as discussed hereinafter.

A. Treatment by Cancer Type

While the state of the art is relatively high with regard to the treatment of specific cancers with specific agents, it has long been underdeveloped with regard to the treatment of cancers broadly. In particular, there is no known anticancer agent which is effective against all cancers. This is why the National Cancer Institute (NCI) has the extensive *in vitro* drug screening program it does. As discussed by the court in In re Brana, 51 F.3d 1560 (Fed. Cir. 1995), *in vitro* assays are used by NCI (such as the P388 and L1210 lymphocytic leukemia tests at issue therein) to measure the potential antitumor properties of a candidate compound. Brana at 1562-63. If success is shown in this initial screening step, this demonstrates that at least one cancer type (e.g., lymphocytic leukemia) is sensitive thereto, and provides the incentive to select it for

further studies to determine its usefulness as a chemotherapeutic agent against other cancer types (lung, breast, colon, etc.) *Id.* at 1567-68. These *in vitro* tests are considered reasonably correlative of success *in vivo*.

Thus, a considerable amount of *in vitro* empirical testing is required, with no *a priori* expectation of success being present, before a candidate anticancer agent can be considered useful against any particular cancer type.

B. Combination Chemotherapy

Furthermore, the unpredictability observed with single agents is compounded when a combination of agents is used. This is summarized by WO 00/61142, at page 1, lines 17-23:

> Combination therapies, while desirable, are a hit or miss proposition. The treatments are typically not additive. In many cases, cross effects and treatment load can result in lower effectiveness for the combinations, than either treatment alone.

This is verified by U.S. Pat. 6,465,448 at col. 1, lines 56-59:

> The design of drug combinations for the chemotherapeutic treatment of cancer should be approached with the goals of 1) finding a combination that is synergistic with and not merely additive to the first compound with respect to the elimination of the tumor, and 2) finding a second drug that does not potentiate the toxic effects of the first therapeutic agent. *These conditions require a great deal of empirical testing* of agents known to have anticancer properties with agents that either may have anticancer properties, or that may augment the first agent in other ways. (Emphasis added).

Thus, when two (or more) agents are used, even more additional empirical testing is required, again with no *a priori* expectation of success.

2. The breadth of the claims

The claim is very broad and inclusive of "proliferative disorders" generally.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction for ascertaining, *a priori*, which cancers, let alone which "proliferative disorders", will respond to treatment.

4. The quantity of experimentation necessary

The lack of adequate guidance from the specification or prior art with regard to the actual treatment of all cancers, let alone all proliferative disorders, in a mammal with the claimed compounds fails to rebut the presumption of unpredictability extant in this art. Applicants fail to provide the guidance and information required to ascertain which particular type of cancer the claimed anticancer combinations will be effective against without resorting to undue experimentation. Applicant's limited disclosure of the treatment of mammary cancer with a combination of a pentafluorobenzene sulfonamide and gemcitibine/paclitaxel (as exemplified in the drawings) is noted but is not sufficient to justify claiming all cancers broadly. No other objective evidence of therapeutic success is provided by the instant specification.

Absent a reasonable *a priori* expectation of success for using a specific chemotherapeutic agent/combination to treat any particular type of cancer, one skilled in the art would have to extensively test many various tumor types. Since each prospective embodiment, and indeed future embodiments as the art progresses, would have to be empirically tested, and those which initially failed tested further, an undue amount of experimentation would be required to practice the invention as its is claimed in its current scope, because the specification provides inadequate guidance to do otherwise.

Obviousness Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Flygare et al (USP 6,482,860 B1).

Patentees disclose using the instantly claimed pentaflurobenzenesulfonamides to treat cancer. See and compare, for example, the compounds of patentees' working examples 6 and 7 with Applicant's preferred compounds of claims 10, 12 and 18. The pentafluorobenzenesulfonamides may be "combined with or used in combination with" other antineoplastic agents such as paclitaxel (col. 20, lines 6-16).

The prior art is not anticipatory insofar as a composition or method of treatment employing an antineoplastic agent in addition to the pentaflurobenzenesulfonamide compound is not specifically exemplified in the form of discrete preferred embodiment or working example. Stated alternatively, some "picking and choosing" from within the four corners of the reference is required to arrive at the instantly claimed combinations. That being said, however, it would certainly have been obvious to do so, motivated by the prior art's clear invitation to do so.

Regarding claims 23-25, it would have been obvious to have administered the pentafluorobenzesulfonamide and antineoplastic agent simultaneously, or one prior to the other. One skilled in the art would have been motivated to vary the order as appropriate to optimize therapy for a particular patient, type of cancer, etc., as is standard in the chemotherapeutic art.

Obviousness-Type Double Patenting Rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 6-13, 17-19 and 23-25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,355,628 B1.

The instant claims broadly recite "antineoplastic agents", including DNA-alkylating agents/intercalators. They thus differ from the conflicting claims, which narrowly recite platinum coordination complexes, such as cisplatin. Platinum coordination complexes are widely commercially available antineoplastic agents which function by DNA-alkylation/intercalation. Accordingly, it would have been obvious to have selected them as specific species within the instantly claimed genera, motivated by the desire to minimize procurement efforts by using easily available agents.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frederick Krass whose telephone number is (703) 308-4335. The examiner can normally be reached on Monday, Tuesday and Thursday from 9am to 5pm, and on Fridays from 11am to 7pm. The examiner is off Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached at (703) 308-4725. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0193.

Frederick Krass
Primary Examiner
Art Unit 1614